

A proposed draft protocol for the European Convention on Biomedicine relating to research on the human embryo and fetus

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Resume

Il s'agit d'un essai pour stimuler le débat sur la recherche sur l'embryon et la rédaction d'un protocole à la Convention européenne de bioéthique. Un tel protocole a en fait été commandé par le Comité des Ministres du Conseil de l'Europe au Comité directeur sur la biomédecine.

Abstract

The objective of this paper is to stimulate academic debate on embryo and fetal research from the perspective of the drafting of a protocol to the European Convention on Biomedicine. The Steering Committee on Bioethics of the Council of Europe was mandated to draw up such a protocol and for this purpose organised an important symposium on reproductive technologies and embryo research, in Strasbourg from the 16th to the 18th of December 1996.

Foreword

The nature of the human embryo and fetus is a long-standing issue in human history. It has anthropological, cultural, religious, ethical, legal and medical implications that are too broad for my present scope.

Although I will not ignore them, I will limit my field of interest to the specific problem posed by the development of new reproductive technologies and related matters. They have produced a new type of embryo: an *in vitro* embryo. They have also enabled more operations to be performed on the fetus *in vivo*. Therefore, some concerns have arisen as to how to protect the embryo and the fetus against undue

scientific interventions, in particular when the embryo is *in vitro* and does not benefit from the physical protection of the woman who bears it.

My objective is very much in line with the present work of the Council of Europe Steering Committee on Bioethics regarding the drafting of a European convention in this field. The committee has in fact been mandated to draft a protocol on research on human embryos and fetuses, although (or because) great divergences exist in member states on the legal status of the human embryo.

Knowing the difficulty of this task, as I have been myself largely involved in the initiative to draft the European convention, I would like through this paper, which presents a study for a draft protocol and an explanatory memorandum, to stimulate debate on this subject. My view is that we urgently need reasonable and well-orientated public debate on the convention, the main text of which was finally adopted by the Committee of Ministers in November 1996.

Before letting the reader form his/her own opinion on this study, I would like to clarify one point regarding what some people would regard as my fundamental presumption, namely the fact that I am going to consider the embryo as a human being.

This consideration should not be viewed as a statement that the embryo has the legal stature of a human being.

I am simply making the following suggestion: let us put aside the controversy about the legal nature of the embryo and let us suppose that the embryo could be regarded as – I do not say *is* – a vulnerable person. Now, we know that experiments on vulnerable persons are legally possible, although more strictly regulated than experiments on non-vulnerable persons. I propose therefore to look at the specific conditions governing these kind of experiments to see if it is possible, *mutatis mutandis*, to apply them to human embryos and fetuses. I then propose to look at the specific scientific or ethical issues arising, which could justify possible exceptions in the application of these specific conditions.

If it proves possible to progress in this way, we will have ensured the highest level of protection possible

Key words

European Convention on Biomedicine; embryo research; vulnerable persons; minimal risk.

Mots-cles

Convention Européenne de Biomédecine; recherche sur l'embryon; personne vulnérable; risque minimal.

for the human embryo, without prohibiting *all* research because the comparison with vulnerable persons, for which research is allowed, will have permitted it.

A last point in this foreword: my approach could appear to some as inconsistent with some (European) domestic legislations, which give free choice to women regarding the termination of pregnancy in the first trimester. I would reply that mine is a legal and international approach to embryo research and does not intend - nor need - to strive for ontological and theological consistency. As regards legal consistency, I question whether protection of the embryo *in vitro* before implantation, and free choice to the mother during the first weeks of pregnancy, are necessarily contradictory. The interests which are in conflict do not have the same value, the same weight. In the second case you have the interest of an existing person opposed to the interest of a person not yet born; in the first case the interest of the embryo, as a symbol of human dignity, is opposed to the interests of science. In no case, in no circumstances, should science prevail over human dignity.

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SECTION 1 – OBJECT AND GENERAL REMARKS

Article 1

The present protocol concerns all research that applies to or may affect the living human embryo or fetus.

Article 2

No research may be set up if it has not been authorised by :

- the woman who is carrying the embryo or the fetus when the research is carried out *in utero* or involves the implantation of an embryo *in utero*;
- the persons with whom the parenting project originated and for whom an embryo has been created *in vitro*;
- in the event of its being impossible to obtain this agreement, of a conflict between the persons who should give it or between the interests of one of them and the interests of the embryo or the fetus, an “ad hoc” representative of the latter, appointed by the legal authority.

Article 3

Research with no direct benefit can only be carried out on human embryos or fetuses in establishments and by persons accredited to do so and for a given period according to procedures fixed by national law.

SECTION 2 – EMBRYO AND FETUS *IN UTERO*

Article 4

During pregnancy, a woman cannot take part in medical research from which her health and/or the health of the embryo or would not benefit in some direct way.

When the anticipated benefit exists only for the woman, the embryo or fetus must only incur the minimum degree of risk connected with this research.

Furthermore, the embryo and the fetus *in utero* cannot be the object of research unless the aim of the research is to ensure their development and if they incur only the minimum degree of risk connected with this research.

Article 5

However, research with no direct benefit for the embryo or the fetus can be carried out if :

- a) its therapeutic, diagnostic or cognitive outcome can be of benefit to other embryos or fetuses that are in this period of life;
- b) the same scientific results cannot be obtained by other means;
- c) the embryo or fetus only incurs a minimum risk;
- d) an independent committee has given its opinion on the research project and the existence of a possible conflict of interest between the woman and the embryo or the fetus;
- e) should there be conflict, an “ad hoc” representative of the embryo or fetus has been appointed by the legal authority.

SECTION 3 – *IN VITRO* EMBRYO

Article 6

No embryo should be procreated *in vitro* for the sole ends of research.

No embryo may be preserved with a view to research by cryopreservation or any other procedure with comparable effects if national law has not determined the rules that should prevail over this preservation.

Article 7

Research on a pre-implantation embryo (*in vitro*) should only be permitted if this research could directly benefit the embryo, in the context of its implantation in the uterus of the woman, its later development or its state of health. The embryo should incur only the minimum degree of risk connected with this research.

Moreover, no research involving the use of techniques of germ cell gene therapy may be carried out if it has not previously been approved by an independent national authority.

Article 8

Exceptionally, research with no direct benefit may be carried out on a pre-implantation embryo:

- a) if it is not likely to be detrimental to it and if it respects the conditions set out in a) b) d) and e) of article 5, or
- b) if its object is to diagnose a particularly serious disorder recognised as incurable.

Article 9

Research on an *in vitro* embryo which cannot be implanted can only be carried out if :

- a) the outcome of the research is the development of techniques of medically assisted procreation or antenatal diagnosis as well as the improvement of knowledge in the field of pathologies that are particularly serious both for humanity and in the field of embryogenesis;
- b) the research is not carried out beyond the 14th day of development;
- c) the research has been subjected to a scientific and ethical assessment by an independent committee.

Explanation of proposed protocol

INTRODUCTION

The choices that inspired the drawing up of this protocol originate in a double hypothesis. First of all, there is the recognition of the legitimacy of biomedical research – which can raise problems of conflict between individual interest and collective interest – and the necessity of determining a legal framework for such research.

In this respect, the protocol follows the ethical and legal principles that have been asserted both by international law and practices and by the internal law of many states.

Secondly, without discussing the legal stature of the human embryo and fetus, we would attempt, as far as possible, to allow them to take advantage, *mutatis, mutandis*, of the condition of greater protection established for so-called vulnerable persons.

Article 1

The protocol covers all research that might have an effect on the embryo or the fetus.

Deliberately, no definition of embryo or fetus is proposed for two reasons. First, when discussing the principles of human artificial reproduction published by the Council of Europe in 1989, members of the committee could never agree on how to define the different steps of development between fertilisation and birth. Second, although we should not ignore the possibility that an embryo could in some circumstances mean a stage of cell division with no embryonic nucleus, this absence of a definition permits us to avoid an endless debate on the concept of the pre-embryo.

It must be possible, therefore, that the research under discussion will affect the physical integrity of the embryo or fetus. However, it may be research of which the embryo or fetus are the direct subjects, or

research such as that carried out on pregnant women, where the embryo or fetus are only indirectly involved.

Finally, research involving embryos or fetuses which are not alive, such as that performed on tissue samples from dead fetuses, is not included in the present protocol, the aim of which is to establish rules for the protection of the physical integrity of human embryos and fetuses.

Article 2

As the embryo or the fetus cannot, hypothetically, consent to research, this article determines the persons entitled to authorise the legally permissible research.

In the absence of parental authority over the embryo or fetus, the following solutions have been proposed:

– in the case of research *in utero* or research involving the implanting of an embryo, it is the woman who has to give her agreement. It might be thought that, when a husband exists, his agreement should also be required. But it has seemed to us that acknowledging a right of veto to the husband, before the birth of the child, could cause problems. As for conflicting interests between the woman and the embryo or the fetus, they are resolved in another way than by the husband's intervention.

– in the case of *in vitro* research, it is the people with whom the parenting project originated (the text does not specify either the number, one person alone or not, or their status, heterosexual couple or not, and consequently refers back to other texts on this point) who must give their agreement.

Finally, in the case of differences between these persons or the interests of one of them and the interests of the fetus or embryo, or in a case where it is impossible to obtain this agreement (the person has died, disappeared or is incapable of expressing him/herself), it is necessary to have the judge appoint an "ad hoc" representative as a protector of the interests of the embryo or fetus.

Article 3

It is important that the public authorities have some control over research with no direct benefit to the embryo or fetus or pregnant woman so as to make clear what is being done and that this is within the general rules that guide the performance of the research. It is therefore clear that the licensing procedure should apply not only in respect of scientific, technical and medical requirements but also in respect of ethical and legal rules that proper practice should follow.

SECTION 2

This section introduces the distinction that runs like a thread through the draft. It is based not on the nature of the research but on the physical situation in which the embryo or fetus is placed: either

in utero, during the pregnancy, or, for the embryo, *in vitro*, which is a new situation – a consequence of the development of the techniques of assisted procreation.

The research considered is obviously not the same in the two situations. But above all, in the case of the embryo or fetus *in vitro*, it is placed in the conditions of a gestation that, unless there is a spontaneous or voluntary termination of the pregnancy, will continue to term.

The present text should be clearly understood as aiming to provide protection for the embryo and fetus against undue scientific or medical interventions. It is not intended to be used as a guide where there is maternal/fetal conflict regarding the termination of pregnancy.

Article 4

This lays down the principle that the research must provide a direct benefit to the embryo, fetus or pregnant woman. (Research with no direct benefit is covered by Article 5 which specifies the exceptions to the rule).

Paragraph 1 firstly envisages the research in which a pregnant woman can take part. The direct benefit can then be expected for the health of the woman and/or the health of the embryo or fetus that she is carrying.

The second paragraph settles the question of a possible conflict of interests between the health of the mother and the health of the embryo or fetus. It limits the research with direct benefit for the woman only to research that does not create for the embryo or fetus concerned a higher than minimum degree of risk. Since research, as in fact any intervention that affects physical integrity, supposes a risk, it is asked that this risk be minimum. This degree is evaluated not "*in abstracto*" but in the light of the research envisaged, which means that a minimal risk can be higher in research 1 than in research 2. However, as no benefit is intended in this situation for the embryo, it is not possible to allow more than a minimal risk as far as the development of the embryo is concerned. A woman could, of course, decide, if the legal conditions were respected, to terminate her pregnancy and then to submit to the research. However, it is not certain, as the procedures for abortion are strictly regulated, that she could decide to accept serious risks for the embryo and then abort, should that appear necessary.

Finally, the third paragraph is aimed at research of which the embryo or fetus is the direct subject. It takes up the issue of the double requirement of direct benefit, which is understood to be ensuring the development of the embryo or fetus, and the minimum degree of risk, again to be evaluated "*in concreto*", proportionate to the advantage expected.

Article 5

As is generally admitted for categories of so-called

vulnerable persons, this article provides for cases where research with no direct benefit could be performed. It specifies the conditions, all of which are taken from, or inspired by, the conditions applied to research on vulnerable subjects, under which such research could take place.

The first of these conditions concerns the final objective of the research. On the one hand it cannot be either commercial, industrial or indeterminate. It must correspond to a therapeutic, diagnostic or (medically or scientifically) cognitive objective.

On the other hand, this final objective is insufficient in itself if it does not have clinical application as an objective: it must be of advantage to other embryos or fetuses that are in the same period of life.

The legitimacy of collective interest is only admitted because it shows that solidarity with regard to potential individual interests has been taken into account.

The second condition, concerning the lack of alternative in the research envisaged, aims, as is required for research on minors, to avoid research being carried out on the embryo or fetus when it could reasonably be done, for example, on an adult or on an animal model.

As the embryo or fetus continues its gestational development, the risk linked to research must be minimal, this requirement is to be assessed "*in concreto*".

The task of assessing whether the preceding conditions have been fulfilled should not be left to the researcher alone or to those who have authority over the embryo or fetus.

Those who make the assessment should ensure that their judgment is enlightened by the opinion of an ethics committee whose composition fulfils the traditionally accepted criteria of independence, multidisciplinary and pluralism. The committee should include, if relevant, a person or persons particularly competent on issues of possible conflict of interest between the embryo or fetus and the woman and/or issues to do with the interest of the embryo, where interest is understood in a wide sense, beyond the interest of the state of health alone.

Finally, in the case of a possible conflict between the interest of the woman and the interest of the embryo or fetus, it is suggested that the legal authority, seeking to guarantee individual liberties but also acting as arbiter of family conflicts, appoint an ad hoc representative whose task would be to ensure that the interest of the embryo or fetus was taken into account.

The appointment and the authority of this representative – the conditions of which should be fixed by national law – should be exercised only in a limited way but for as long as a possible conflict of interest exists.

SECTION 3: THE *IN VITRO* EMBRYO

The techniques of medically assisted procreation have had the effect of creating for the embryo a new

state, the state of being an *in vitro* embryo, whose conception is extra-corporeal. Furthermore, placed outside the uterus of a woman, the embryo cannot carry a gestation to full term. Can this double observation make impossible a reasoning comparable to the one applied to *in utero* research? The articles in this section aim to show that it is possible to envisage for *in vitro* research bases that are identical to those for *in utero* research, insofar as their implementation is the object of specially prepared rules.

Article 6

Dealing with the question of research on an *in vitro* embryo, in particular regarding research with no direct benefit, takes on a very different meaning when the first cause of the death of an embryo is due to its state (post-implantation or suffering from serious abnormalities) and not to human intervention.

Indeed, it is the impossibility of satisfying the condition of minimum risk, since it would always be fatal, that leads to immediate rejection of research on an *in vitro* embryo. It is therefore important that the researcher should not be the instigator of this risk, or rather this certainty.

This is why it will be prohibited to procreate an embryo only for research purposes.

We are aware that here begins the point where consensus seems particularly uneasy. To this proposed rule researchers would object, with pertinent scientific arguments, that we need to procreate embryos for research purposes, but opponents would question the rule on casuistic grounds. Also, others would say: "You ban procreating embryos only for research purposes because it would imply that man is the investigator of a 'planned death' of the embryos concerned. Yet in compensation you authorise research on 'non viable' embryos. But you do not wonder why you get such embryos. Yet you get such embryos because reproductive technologies, which are man-run technologies, have developed. Where then is the difference?"

We do not share this last view which would imply, for consistency, a ban, as in Ireland, on any practice that would not lead to the transfer into a woman's womb, of all the embryos procreated. This would be, of course, contrary to the inviolability of the human person. But we also do not share the view that the principle of human dignity should not inspire provisions which could be binding for researchers.

As a lesser drawback, we would admit research on "non viable" embryos but we would refuse to allow scientists to procreate embryos as raw material for their work.

We shall examine later (article 9) the question of the legitimacy of research on *in vitro* embryos that are sure to die from other causes.

Finally, the second paragraph, in order to avoid the proliferation of the places for preservation and the number of embryos "stocked frozen", sets as a

principle that no preservation of this type will be possible with the aim of research, if the national legislator does not regulate the conditions for setting up and operating embryo banks. The national legislator can, of course, extend the field of application of his regulations to preservation directly linked to medically assisted procreations, which is, however, outside the field of application of the present protocol.

Article 7

Is it possible to talk, where the *in vitro* embryo is concerned, of research with a direct benefit? This would suppose, at least, that the embryo is destined to be implanted in the uterus of the woman, which, in turn, presupposes that the woman accepts the transfer of the embryo. However, the text leaves open the question as to whether the decision could be objected to on the grounds of the interest of the embryo. This is of limited interest for those states where termination of pregnancy is left, during the first trimester, to the choice of the mother.

Therefore the only embryos concerned are those that have not exceeded *in vitro* a stage of development beyond which their implantation cannot be envisaged, hence the term "pre-implantation" that qualifies such an embryo. As for the direct benefit for the embryo concerned, it can only be in promoting its implantation, its later development or its state of health.

The risk incurred, that some people could accept at a degree higher than minimum, considering that it is necessary to promote the development of an embryo, should not, in our opinion, exceed the first degree of risk. A balance has to be found between, on the one hand, promoting the development of an embryo and, on the other hand, not creating for it a degree of risk that could lead to the emergence of serious abnormalities.

Finally, admitting that research on an *in vitro* embryo may be envisaged if it has a direct benefit for the (present or future) health of the embryo leads to questions about the possibility of implementing techniques of germ cell gene therapy.

The proposed draft protocol does not provide for forbidding these techniques *a priori* and in an absolute way, for it does not subscribe to the hypothesis that any modification of the germ line would endanger the integrity of humanity and the human species.

On the contrary, the draft is based on the idea that very serious illnesses, such as Tay-Sachs disease or Lesh-Nyhan disease are objective ills: if we have the power to palliate these misfortunes, which imperil a person's ability to reason and his freedom, and by acting do not sacrifice anything fundamental, then refraining from action would be unethical.

The particular consequences of germ cell gene therapy, the need to master the technique and the feeling that it evokes in the public, lead however, to

a subordination of the practice of research to a system of prior authorisation on a national level. The expression "independent authority" has been proposed in order to leave a margin of assessment to the contracting parties. The authority can be either an authority specialised in issues concerning life sciences, for example a national ethics committee, or an *ad hoc* commission, or even a country's legislature.

Article 8

As far as research with no direct benefit on pre-implantation embryos is concerned, two opposing positions can be envisaged. The first, because of the destiny planned for those embryos to be implanted, would consist in forbidding all research with no direct benefit. The second would be to authorise this research on certain conditions, but not to allow the implantation of the embryos concerned, given the risk of producing serious abnormalities.

The text of the draft proposal puts forward a solution between the two positions: ie one which does not prevent the implantation of these embryos, yet which carries the reservation that the research should not be detrimental to them (whether it be observation or the study of cultures, for example) and that the strict conditions provided for *in utero* research with no direct benefit, should be respected.

To this middle course the text adds the possibility of carrying out a pre-implantation diagnosis solely of particularly serious disorders that are incurable at the time of the diagnosis. This involves diseases for

which the legislator admits, in general, that recourse might be had to termination of pregnancy, sometimes even beyond the legal date set for termination of pregnancy for social reasons.

Article 9

Here we are in the situation where the non-viability and the death of the embryo are not due to the intervention of the researcher but to the state of the embryo, either because it was not able to be implanted in time (the woman gave up her project or was not available) or because serious abnormalities, which it carries, have made implantation impossible.

Mutatis mutandis, a parallel can be established with the issue of research on individuals who are about to die. The essential rule is to ensure the respect due to the human dignity of the embryo, respect that imposes a limited amount of research both because of its object and because of the time during which it can take place. This condition of time (the 14th day of development) also makes it possible to check that the research will not lead to the embryo being affected at a more advanced stage of development.

Judge Christian Byk is Associate Professor at the University of Poitiers, France and Secretary General of the International Association of Law, Ethics and Science. He was the French representative to the now titled Steering Committee on Bioethics (1983-1991) and Special Adviser to the Secretary General of the Council of Europe (1991-1993).

News and notes

Teaching Research Ethics: Fourth Annual Workshop

The fourth annual "Teaching Research Ethics" workshop will convene at Indiana University, June 25-28, 1997. Registrations are now being accepted. Attendance at the workshop will be limited to 30-45 participants, and the workshop fee is \$300. Two additional, larger, meetings will be held on Saturday, June 28.

Workshop sessions will cover ethical theory, human subjects research, animal subjects research, responsible data management, collegiality and authorship, investigating scientific misconduct, conflicts of interest, and pedagogical techniques in teaching research ethics (including the use of case studies).

On Saturday morning, a panel of faculty members and administrators from a variety of universities will present Model Curricula in Research Ethics. This session will provide an ideal opportunity to learn about a number of different programmes and courses in research ethics. Registration is required, but there is no fee to attend the panel.

Following the panel, R Lee Zasloff, Associate Director of the Center for Animal Alternatives at the University of California-Davis, will lead a day-long seminar on Alternatives to Animal Use in Education, Research, and Testing. Registration is required, and a \$50 fee will be charged of persons who did not attend the workshop.

Financial support for the workshop comes from Indiana University-Bloomington, Michigan State University, Northwestern University, The Ohio State University, Purdue University, University of Illinois-Urbana/Champaign, University of Iowa, University of Michigan, University of Minnesota, and University of Wisconsin-Madison.

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